REMARKS

I. Preliminary Comments and Discussion of Amendments

Applicant, through the undersigned attorney wishes to thank the Examiner for the courtesy shown during the telephonic interview conducted June 8, 2004. During that Interview differences between the subject matter of the invention and the disclosures of the Lundin and Khanna references were discussed. In addition, the Declaration of Dr. Horton submitted October 22, 2001 as it applied to the disclosures of Lundin and Khanna was also discussed. Finally, the duplicative nature of claims 17 and 19 and the cancellation of claim 19 were discussed.

The present invention is directed to specific binding assays in which the presence of an intracellular analyte in a sample is assayed for by steps including reaction of a specific binding partner for the analyte with the analyte to form a specific binding partner-analyte complex and detection of that complex. (e.g., antigens and antibodies)

More particularly, the method of the invention includes the steps of mixing a sample of cells with a cell lysis agent to provide a lysed cellular sample, mixing the lysed cellular sample with a cyclodextrin sequestrant for the cell lysis reagent, and performing the specific binding assay in the presence of that sequestrant. The purpose of the sequestrant is to prevent the cell lysis reagent from adversely affecting the binding reaction between the analyte and its specific binding partner.

II. Outstanding Rejections

Claims 1-2, 4-5, 8, 10, 14 and 16-20 stand rejected under 35 U.S.C. §103 (a) as being obvious over Lundin, U.S. Patent No. 5,558,986 in view of the Khanna U.S. Patent No. 5,032,503.

Claims 6 and 9 stand rejected under 35 U.S.C. §103 (a) as being obvious over Lundin in view of Khanna and in further view of Cook (2) WO 94/26413.

Claims 7 and 11-13 stand rejected under 35 U.S.C. §103(a) over Lundin in view of Khanna and further in view of Brown, U.S. Patent No. 5,739,001.

Claim 21 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Lundin, in view of Khanna, and further in view of Edmonds, U.S. Patent 6,159,750.

Claims 17 and 19 stand objected to as being substantial duplicates of one another.

III. Patentability Arguments

The present rejections based upon Lundin and Khanna, either together or in combination with other references, should be withdrawn because the art fails to teach that cyclodextrin can neutralize the effects of detergent on a specific binding assay when the detergent is so strong that it can lyse cell samples.

Lundin is directed to enzyme mediated amplification assays in which a cyclodextrin is used as a sequestrant for a cell lysis reagent. Typical enzyme-mediated reactions include firefly luciferase assays, polymerase chain reaction (PCR) nucleic acid amplification, and restriction enzyme digestions in which an enzyme-mediated reaction amplifies the record of the presence of the involved enzyme through the catalysis of the enzymatic reaction to produce a product. Because an enzyme is not consumed in a catalytic reaction the reaction will continue and product will be produced until the reactants are exhausted.

Khanna is directed to specific binding assays in which cyclodextrin is used to neutralize the surfactant interference with specific binding pair interaction caused by the presence of low levels of detergent used to keep normally interacting components of a specific binding pair apart in a single liquid reagent. Khanna teaches away from the use of detergent levels sufficient to lyse cell samples and prescribes the use of low concentrations of surfactant (i.e., "[d]esirably, the concentration [of surfactant] will be insufficient to denature the specific binding pair members the sample analyte or any other assay reagents." (col. 4, lines 8-11).

Neither Lundin nor Khanna anticipate the claims of the present invention which involves conducting a specific binding assay after conducting a cell lysis step using sufficient detergent to lyse cells. As discussed at the Interview, the observation that a

cyclodextrin can be effective in the enzyme-mediated amplification assay of Lundin does not imply that it would be effective in the much more sensitive environment of a specific binding assay.

While the enzyme-mediated amplification assay of Lundin benefits from the fact that non-inactivated enzyme is not "consumed" in a reaction and an enzyme-mediated reaction will continue until the reactants are consumed; such is not the case in a specific binding assay in which the amount of specific binding partner-analyte complex "product" produced will be limited to the amount of biologically active analyte. (See paragraphs. 6 and 7 of the Declaration of Dr. Jeffrey Horton filed October 22, 2001)

Dr. Horton further concluded that:

> ...the utility of a cyclodextrin sequestrant to provide positive assay results in an enzyme-mediated assay would not lead one of ordinary skill in the art to conclude that similar improvements could be attained in a specific binding assay. ... Accordingly, it would not have been clear to one of ordinary skill in the art that incorporation of a cyclodextrin sequestrant would solve the inactivation problem caused by cell lysis reagents. (Paragraph 8, Horton Declaration)

For this reason the obviousness rejection over Khanna and Lundin should be withdrawn. Further, the additional references, while directed to certain aspects of the dependent claims fail to make up for the deficiencies of independent claims 1 and 14. Specifically, Brown is directed to the use of a specific binding assay in a single reaction vessel. Edmonds discloses a specific binding assay using fluorescence polarization assay and Cook (2) WO 94/26413 relates to multiwell scintillation assays but teaches away from cell lysis with a detergent but none of these teach that incorporation of a cyclodextrin would solve the inactivation problem caused by cell lysis reagents in a specific binding assay.

CONCLUSION

Applicant submits that this case is in a condition for immediate allowance. For the foregoing reasons Applicant respectfully requests reconsideration and allowance of rejected claims 1-2, 4-5, 8, 10, 14 and 16-18 and 20. Should the Examiner wish to discuss

Application No.: 09/027,654 Docket No.: 28911/34561

any issues of form or substance in order to expedite allowance of the pending application, she is invited to contact the undersigned attorney at the number indicated below

Dated: **June 9, 2004**

Respectfully submitted,

By _____
Jeffrey S. Sharp
Registration No.: 31,879
MARSHALL, GERSTEIN & BORUN LLP
233 S. Wacker Drive, Suite 6300
Sears Tower
Chicago, Illinois 60606-6357
(312) 474-6300
Attorney for Applicant